

Find Functions: KEGG Orthology Terms & Pathways

From the **Find Function** top-level menu, the **KEGG** option on the second-level menu leads to the **KEGG Orthology Terms and Pathways** browser, as shown in Figure 1(i). KEGG Orthology (KO) terms identify orthologous groups of genes organized using the BRITE functional hierarchy (http://www.genome.jp/kegg/brite.html - see Figure 1(ii)).

(i) KEGG Orthology (KO) Terms and Pathways

KEGG Orthology (KO) Terms Based on **BRITE Hierarchy**
 KEGG Pathways via KO Terms

01 Metabolism
02 Overview
 03 [Carbon metabolism](#)
 03 [2-Oxocarboxylic acid metabolism](#)
 03 [Fatty acid metabolism](#)
 03 [Biosynthesis of amino acids](#)
 03 [Degradation of aromatic compounds](#)
02 Carbohydrate metabolism
 03 [Glycolysis / Gluconeogenesis](#)
 03 [Citrate cycle \(TCA cycle\)](#)
 03 [Pentose phosphate pathway](#)
 03 [Pentose and glucuronate interconversions](#)
 03 [Fructose and mannose metabolism](#)
 03 [Galactose metabolism](#)
 03 [Ascorbate and aldarate metabolism](#)
 03 [Starch and sucrose metabolism](#)
 03 [Amino sugar and nucleotide sugar metabolism](#)

(ii) KEGG BRITE Database
 Functional hierarchies and binary relationships of biological entities

Menu: [PATHWAY](#) [BRITE](#) [MODULE](#) [KO](#) [GENOME](#) [GENES](#) [LIGAND](#) [DISEASE](#) [DRUG](#) [DBGET](#)

Enter keywords ☐ KEGG identifiers only

[New BRITE files | Update history]

Functional Hierarchies

KEGG BRITE is a collection of manually created hierarchical text (htext) files capturing functional hierarchies of various biological objects, especially those represented as KEGG objects. In contrast to KEGG PATHWAY, which is limited to molecular interactions and reactions, KEGG BRITE incorporates many different types of relationships.

(iii) KEGG Pathway Details
 Details for Pathway: Citrate cycle (TCA cycle)

[KO Terms in Pathway](#) [Save to My Workspace](#) [View Map for Selected Genomes](#)

KEGG Orthology (KO) Terms in Pathway

[Add Selected to Function Cart](#) [Select All](#) [Clear All](#)

Filter column: KO Term ID Filter text

Export Page 1 of 3 << first < prev 1 2 3 next > last >> 100

Select	KO Term ID	KO Name	Definition	KO Module ID	KO Module Name	Gene
<input type="checkbox"/>	KO:K00024	mdh	malate dehydrogenase [EC:1.1.1.37]	M00011	Citrate cycle, second carbon oxidation, 2-oxoglutarate >= oxalosuccinate	
<input type="checkbox"/>	KO:K00024	mdh	malate dehydrogenase [EC:1.1.1.37]	M00020	Incomplete reductive citrate cycle, aspartate >= oxoglutarate	
<input type="checkbox"/>	KO:K00024	mdh	malate dehydrogenase [EC:1.1.1.37]	M00740	Methylsuccinate cycle	

Figure 1. KEGG Orthology Terms and Pathways

Clicking on any pathway names shown in Figure 1(i) will lead to a **KEGG Pathway Details** page as shown in Figure 1(iii) with all the KO terms associated with this pathway listed in a table display. Users can select a subset of the KO terms to be added to the Function Cart or Workspace (in the **Save to My Workspace** tab) for further analysis.

The **View Map for Selected Genomes** tab in the KEGG Pathway Details page (Figure 1(iii)) allows users to view how genes of selected genomes are mapped to the functions in this pathway. For example, select to add *Acidianus hospitalis* W1 (in Figure 2(i)) and then click the "View Map" button to lead to a KEGG map display highlighted with functions associated with genes of this genome (Figure 2(ii)). To see the actual gene list (Figure 2(iii)), select the colored EC number square on the KEGG map.

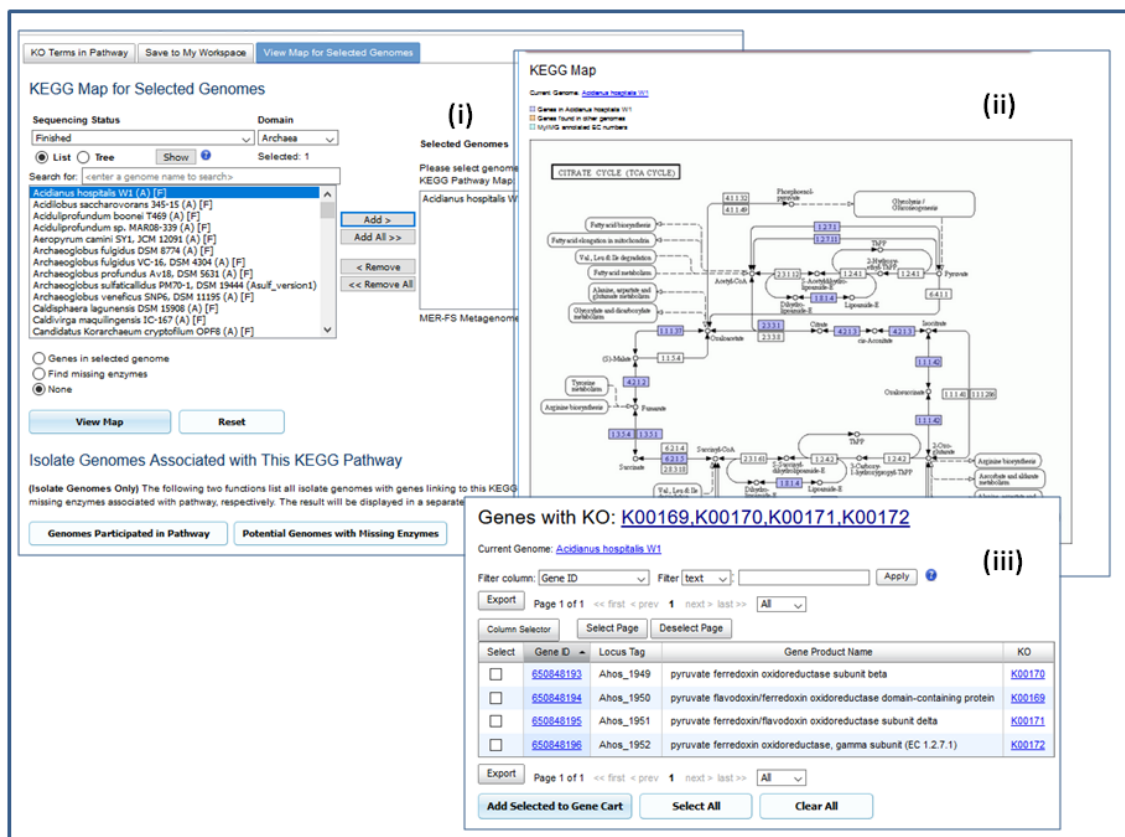


Figure 2. KEGG Map with Selected Genome.

There are two additional functions in the **KEGG Map for Selected Genomes** page (the two buttons in the lower part of Figure 2(i)):

- **Genomes Participated in Pathway:** The function lists all isolate genomes that have genes associated with KO term or enzymes in the pathway (Figure 3(i)). (Note that there is a limitation on numbers of genomes to be displayed.)
- **Potential Genomes with Missing Enzymes:** Since IMG uses higher cut-off values for gene to KO/enzyme association (see SOP for more details), there can be additional gene-enzyme associations that are not used in IMG gene function annotation. The function lists all isolate genomes having such "missing" associations (Figure 3(ii)). This is related to the finding missing enzymes function to be described below. (Note that there is a limitation on numbers of enzymes to be checked and a limitation on numbers of genomes to be displayed. Such limitations were set to avoid browser timeout.)

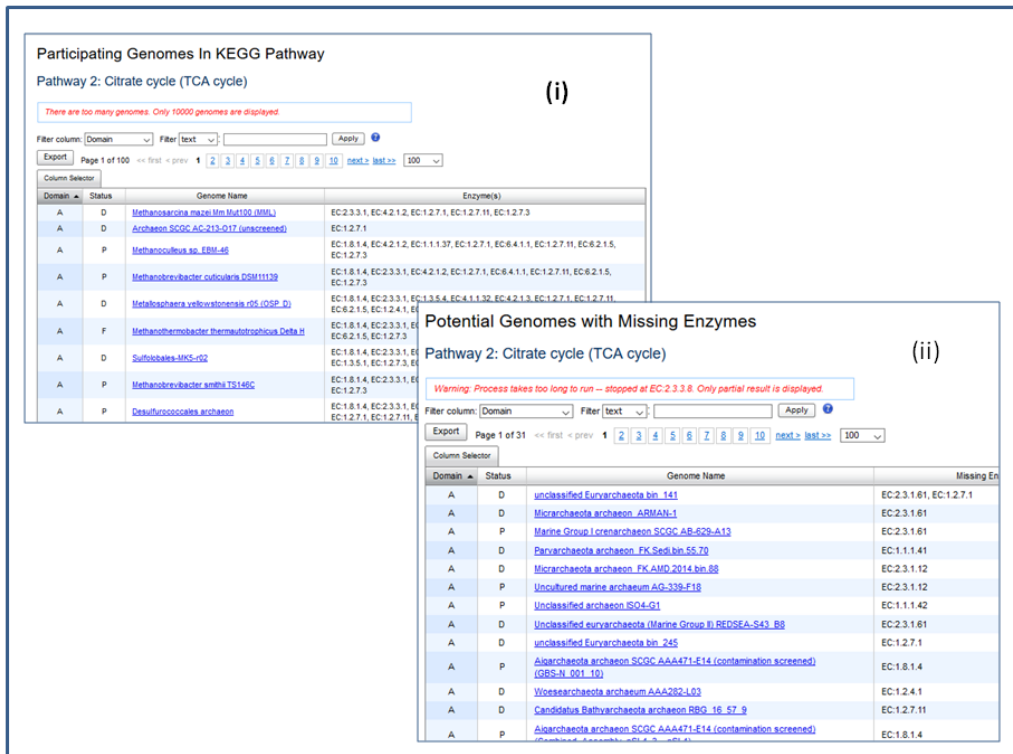


Figure 3. Participating Genomes in KEGG Pathway and Potential Genomes with Missing Enzymes.

For example, using the Potential Genomes with Missing Enzymes function described above, we find that *Halococcus agarilyticus* 197A may have missing enzyme annotations in KEGG Pathway *Styrene degradation*. So we select *Halococcus agarilyticus* 197A and select the "Find missing enzymes" option to view map (see Figure 4(i)). The KEGG map display in Figure 4(ii) shows two potential missing enzymes EC:3.5.5.1 and EC:3.5.1.4 (colored in light green). Selecting EC:3.5.1.4 and using homologs to *Halobacteria* we find 4 potential genes in *Halococcus agarilyticus* 197A that can be annotated with EC:3.5.1.4 (see Figure 4(iii)). Potential genes can be selected to add into the Gene Cart for further analysis. It is also possible to use MyIMG annotation feature to any of the 4 genes to add new gene-enzyme annotations. (See MyIMG User Guide for more detail on MyIMG annotations.)

KO Term Detail (iii)
 KO:K00002: alcohol dehydrogenase (NADP+) [EC:1.1.1.2] (AKR1A1, adh)

KO Modules and Pathways

KO Module ID	KO Module Name	Pathway ID	KEGG Pathway Name
M00014	Glucuronate pathway (uronate pathway)	4	Pentose and glucuronate interconversions

Genome List

Domains(D): * = Microbiome, B = Bacteria, A = Archaea, E = Eukarya, P = Plasmids, G = GFragment, V = Viruses, Genome Completion(C): F = Finished, P = Permanent Draft, D = Draft

KEGG Orthology (KO) Term Isolate Genomes (ii)
 KO Term: AKR1A1, adh alcohol dehydrogenase (NADP+) [EC:1.1.1.2]

Domains(D): * = Microbiome, B = Bacteria, A = Archaea, E = Eukarya, P = Plasmids, G = GFragment, V = Viruses, Genome Completion(C): F = Finished, P = Permanent Draft, D = Draft

Table (i): KO List

Select	KO ID	KO Name	Isolate Genome Count	Metagenome Count
<input type="checkbox"/>	KO00001	alcohol dehydrogenase [EC:1.1.1.1] (E1.1.1.1, adh)	2,140	13555
<input type="checkbox"/>	KO00002	alcohol dehydrogenase (NADP+) [EC:1.1.1.2] (AKR1A1, adh)	860	8852
<input type="checkbox"/>	KO00003	homoserine dehydrogenase [EC:1.1.1.3] (E1.1.1.3)	574034	13884
<input type="checkbox"/>	KO00004	(R,R)-butanediol dehydrogenase / meso-butanediol dehydrogenase / diacetyl reductase [EC:1.1.1.4 1.1.1.- 1.1.1.303] (BDH, butB)	8349	10137

Figure 5. KO List and KO Term.

Clicking on a (meta)genome count will lead to a list of (meta)genomes having genes annotated with this KO term (see Figure 5(ii)). Genomes can be selected to add to Genome Cart for further analysis. Clicking on any gene count to view the actual gene list.

Clicking on a KO ID will lead to a KO Term Detail page showing KO Modules and Pathways, as well as genomes associated with the KO term (see Figure 5(iii)).

KEGG Module

IMG users can view and select all KEGG modules in IMG by selecting the **KEGG Module List** submenu under **KEGG** menu. **KEGG Module List w/ Stats** is similar to **KEGG Module List** except that each KEGG Module is associated with (pre-computed) counts of isolate and metagenomes having genes associated with this KEGG Module (see Figure 6(ii)). KEGG Modules are not selectable for analysis.

KEGG Module Details (iii)

Module ID: M00608
 Module Name: 2-Oxocarboxylic acid chain extension, 2-oxoglutarate => 2-oxoadipate => 2-oxopimelate => 2-oxosuberate
 Module Type: Pathway
 Link to KEGG: [2-Oxocarboxylic acid chain extension, 2-oxoglutarate => 2-oxoadipate => 2-oxopimelate => 2-oxosuberate](#)
 Definition: K10977 K16792+K16793 K10978
 KO Terms in Module: [Save to My Workspace](#) [View KO Module Map](#)

KEGG Module Genome List (ii)

M00608: 2-Oxocarboxylic acid chain extension, 2-oxoglutarate => 2-oxoadipate => 2-oxopimelate => 2-oxosuberate

Domains(D): * = Microbiome, B = Bacteria, A = Archaea, E = Eukarya, P = Plasmids, G = GFragment, V = Viruses.
 Genome Completion(C): F = Finished, P = Permanent Draft, D = Draft.

KEGG Modules (i)

Module ID	Module Name	Module Type	Definition	Isolate Genome Count	Metagenom Count
M00302	2-Aminoethylphosphonate transport system	Complex	K11081+K11082+K11083+K11084	4239	4635
M00608	2-Oxocarboxylic acid chain extension, 2-oxoglutarate => 2-oxoadipate => 2-oxopimelate => 2-oxosuberate	Pathway	K10977 K16792+K16793 K10978	931	6948
M00376	3-Hydroxypropionate bi-cycle	Pathway	K02160+K01961+K01962+K01963 K14468 K14469 K15052 K05606 (K01847 K01848+K01849) K14471+K14472 K00239+K00240+K00241 K01679 K08691 K14449 K14470 K09709	53643	15113

Figure 6. KEGG Modules.

Clicking on a (meta)genome count will lead to a list of (meta)genomes having genes associated with this KEGG Module (see Figure 6(ii)). Genomes can be selected to add to Genome Cart for further analysis. Clicking on any gene count to view the actual gene list.

Clicking on a Module ID will lead to a KEGG Module Details page showing KEGG Module definition and KO terms associated with the module (see Figure 6(iii)). Users can select KO terms to add to the Function Cart or to the Workspace (in the **Save to My Workspace** tab).

The **View KO Module Map** tab in the **KEGG Module Details** page (Figure 7(i)) allows user to select genomes to view on the Module Map. Click on the "Select Genome(s) to View on Map" button to perform genome selection as shown in Figure 7(ii). The "Show Map" button will lead to a colored KEGG Module Map with genomes mapped on KO terms in the module (Figure 7(iii)).

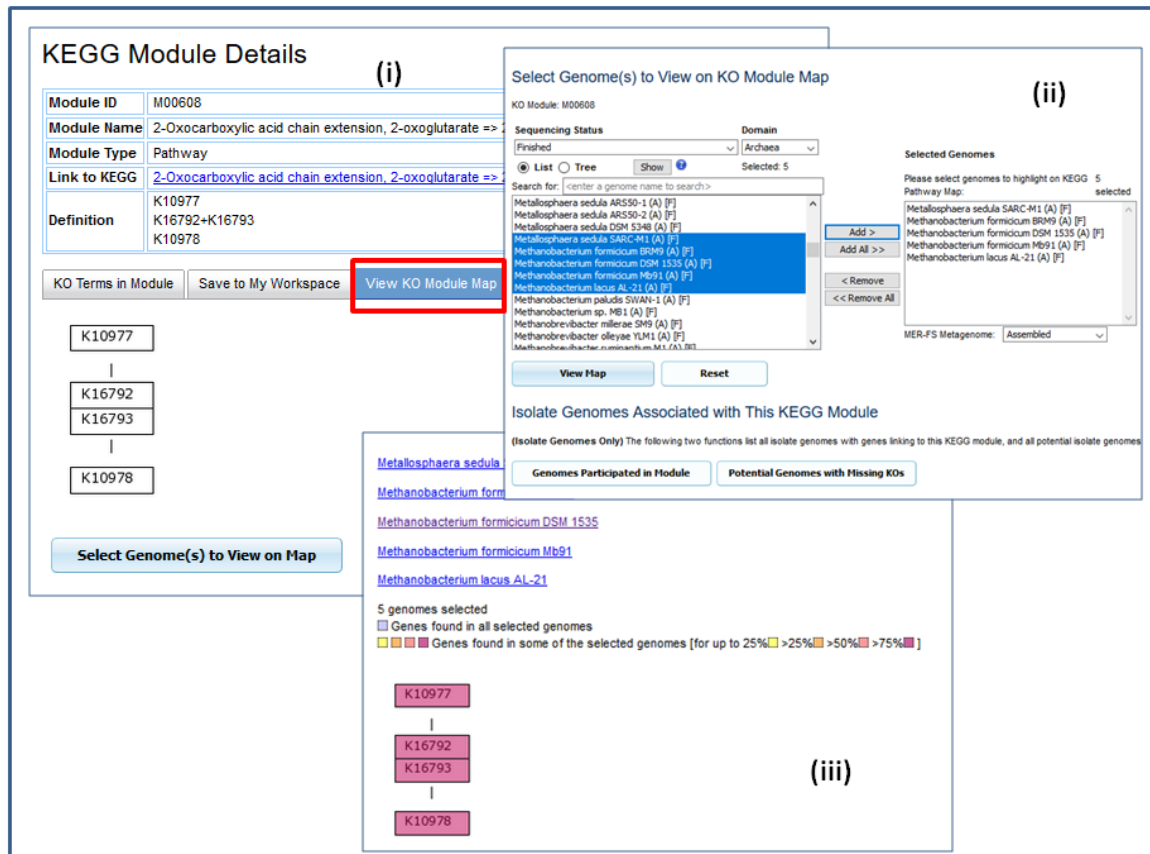


Figure 7. View Genomes on Selected KEGG Module Map.

There are also two additional functions "Genomes Participated in Module" and "Potential Genomes with Missing KOs." They are the corresponding functions of "Genomes Participated in Pathway" and "Potential Genomes with Missing Enzymes" in KEGG pathways as described above.

Orthology KO Terms

This submenu leads to the same KEGG Orthology (KO) Terms and Pathways page shown in Figure 1(i).

Pathways via KO Terms

This submenu leads to the same KEGG Orthology (KO) Terms and Pathways page shown in Figure 1(i) but with **KEGG Pathways via KO Terms** displayed.